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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
03/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/569,160	ASMUSSEN ET AL.	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-12,14-24 and 27-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-12,14-24 and 27-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response dated 12/28/09.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 7-9, 11, 12, 14-24, and 27-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Yang et al (US 2003/0107149 hereafter '149) in view of Gilis et al (USPN 6,099,863 hereafter '863).

The '149 patent discloses a thin oral film formulation comprising an active agent and a polymer [0017-0021]. The thin films can be made with or without mucoadhesive components [0155]. The films may be introduced to a liquid and dissolves due to their tendency to dissolve quickly and administered as a beverage effectively not adhering to a mucosal surface [0157]. The film comprises polymers, active agents and additives in a wide range of concentrations. In Example E, the polymer is present in an amount up to about 46% based on a dried film with no

more than 6% water [Table 1]. The drug content is about 27% while the wetting agents such as Tween 80 are present in a concentration of about 17% [Table 1]. The films can be multilayered where at least one layer comprises the active agent [0132]. The films dissolve in the oral cavity, including the buccal, gingival and sublingual mucosa and as such can be used to deliver active agents to those areas [0093, 0156]. The films dissolve quickly in an aqueous environment [0157]. However the film may comprise a layer that delays the release of the drug [0155]. The films have a thickness from 500 microns to 1500 microns, or up to 0.15 mm [0152]. The film comprises fillers, colorants, plasticizers and the like [01174-0130]. Cholinesterase inhibitors can be included in the film formulation [0099].

The reference differs from the instant claims in that although cholinesterase inhibitors can be included in the formulation they are not specifically named by the '149 application. These compounds are well known in the art, specifically in the art of orally dissolvable dosage forms. This can be seen in the '863 patent.

The '863 patent discloses a fast dissolving galanthamine formulation (abstract). The formulation comprises a carrier matrix where the active agent is present in an amount from 2 to 10%, with the support matrix up to 93% (col. 3, lin. 50-65). The support matrix includes a polymeric disintegrants as well as microcrystalline cellulose (***Ibid.***). The formulation comprises other excipients lubricants and fillers (Examples). The formulations dissolve in the oral cavity and begin to deliver their active payloads within 5 minutes (Example 6). The formulation can be used to treat chemical dependency such as nicotine dependency and cravings, Alzheimer's Dementia and associated symptoms and side effects, including impaired memory, negative sides effects of psychotropic treatments such as benzodiazepine and general mania, chronic fatigue

syndrome (col. 1, lin. 43-65). It would have been obvious to include the galanthamine salt of the '863 patent into the thin oral films of the '149 patent since the '149 reference is suggestive of cholinesterase inhibitors and discloses fast dissolving oral dosage forms. The combination would have been obvious following the suggestions of the '149 application and teachings of the '863 to quickly deliver the compounds orally. The combination would have been obvious to on of ordinary skill in the art in order delivery a quick relief to those suffering from chemical dependency.

Regarding the specific concentration ranges of the instant claims, it is the position of the Examiner that such limitation do not distinguish over the prior art. The '149 patent discloses a thin film composition comprising a polymer and an active agent. The polymer and active agent are present in concentration ranges which overlap the instant claims. Specifically the active agent concentration can be as high as 27%, based on a dried film with at most 6% water. One of ordinary skill in the art would be motivated to optimize the range in order to achieve a more potent or effective dosing effect. This optimization would be achieved through routine experimentation and would be obvious to one of ordinary skill.

Regarding the dissolution profile recited in the claims 30 and 31, it is the position of the Examiner that such limitations would be inherently met by the prior art. The claims recite a film comprising a galanthamine compound and a polymer dissolves within a specified time and achieves a specific plasma level. However the dissolution rate is a functional limitation that does not define a structure. The functional limitation is solely dependent on the compositional components of the claim, and as such since the only compositional components of the claim are a thin film comprising a galanthamine compound and a polymer, the compositional components

art met. Since the same compounds must have the same features and function, the thin film of the prior art combination that comprises a galanthamine compound and a polymer inherently will dissolve within 30 minutes and achieved an optimal plasma concentration.

One of ordinary skill in the art would have been motivated to combine the galanthamine salt of the '863 patent into the film composition of the '149 reference in order to quickly deliver the compounds to patients suffering from chemical dependency. The combination would have been obvious since both references disclose oral delivery of cholinesterase compounds in compositions comprising similar amounts of the active agents and polymer matrix components. Both references also disclose similar carrier matrices comprising flavors, filers and plasticizers. Both formulations are designed to dissolve quickly to overcome the limitation of dosage forms that require swallowing. It would have been obvious to combine the prior art with an expected result of a stable film formulation useful in treating chemical dependency.

Claims 1-3, 7-12, 14-24, 27-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Yang et al (US 2003/0107149 hereafter '149) in view of Gilis et al (USPN 6,099,863 hereafter '863) and Uekama et al (USPN 5,904,929 hereafter '929).

As discussed above the combination of the '149 and '863 patent would provide a buccal film formulation comprising cholinesterase inhibitors and a polymer matrix that dissolves quickly in the oral cavity. The combination is however silent o to further cholinesterase inhibitors, although the '149 suggests that these compounds can be present in the plural. It would be obvious to add additional similarly acting compounds to the formulation in order to increase the effectiveness of the dosage form. These other compounds are well known tine hart as seen in the '929 patent.

The '929 patent discloses oral formulations comprising a range of active agents including parasympathomimetics such as galanthamine, neostigmine and tacrine (col. 6, lin. 20-23). The dosage forms include trans-mucosal or transdermal films, or tablets (col. 4, lin. 1-20). The formulation further comprises microcrystalline cellulose, and hydroxypropylcellulose (Example 13). It would have been obvious to add these other cholinesterase inhibiting compounds to the combination of the '149 and '863 films in order to increase the effectiveness. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. *See* In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

It would have been obvious to combine the other cholinesterase inhibitory compounds of the '929 patent into the combination of the '149 and '863 reference since each patent discloses a similar composition comprising the same active agents, in similar polymeric matrices that are all delivered orally. This combination would have been obvious in order to increase the effectiveness of the dosage form in treating chemical dependency. One of ordinary skill in the art would have been motivated to combine the prior art with an expected result of a buccal film useful in the treating chemical dependency.

Response to Arguments

Applicant's arguments filed 12/28/09 have been fully considered but they are not persuasive. Applicant argues that:

The combined references do not suggest or discloses a thin film dosage form that is water soluble by not mucoadhesive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Regarding this argument, Applicant is directed to [0155-0157] of the '149 patent where mucoadhesive components are merely optional. The thin films are disclosed as water soluble that dissolve completely in liquids and can be delivered via a beverage dosage form. While galanthamine or its derivatives are not exemplified by the patent, cholinesterase inhibitors are disclosed as useful active agents [0099]. It would have been obvious to include the galanthamine compounds of the '863 patent into the thin film of the '149 since both compounds disclose similar excipients and deliver their active agents orally. It would have been prima facia obvious to substitute a specific cholinesterase inhibitor into the general film formulation of the '149 in order to quickly deliver the compounds. Since the genus has been suggested, it would have been within the level of skill in the art to make the simple substitution of the species the '863 patent. The combination would have been obvious since both references disclose oral delivery of cholinesterase compounds in compositions comprising similar amounts of the active agents and polymer matrix components. Both references also disclose similar carrier matrices comprising flavors, filers and plasticizers. Both formulations are designed to dissolve quickly to overcome the limitation of large dosage forms that require dissolution in the gastrointestinal tract.

Applicant argues that there would be no motivation to combine the prior art in order to form a buccal delivery film that is not mucoadhesive. The '149 patent discloses buccal delivery for the thin films of the invention [0093, 0156]. The '863 patent provides an oral formulation of

galanthamine, while the '929 patent provides a transmucosal formulation. Each patent provides a similar formulation with comparable components within the same field of endeavor in order to deliver active agents orally, specifically buccally. This would have been obvious since each patent discloses similar components such as microcrystalline cellulose, and similar active agents such as cholinesterase inhibitors. It would have been obvious to combine the active agents of the '863 and '929 patent into the thin film platform of the '149 patent since it is suggestive of delivering cholinesterase inhibitors in a similar fashion, specifically buccally. There would have been a reasonable level of success since each patent provides a successful formulation that delivers its payload to the patient. As such the combination of prior art would have been obvious to one of ordinary skill in the art. It is the position of the Examiner that the combination of the prior art would disclose methods of buccal delivery. For these reasons the claims remain obviated.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. The new rejection is based on the additional new claims and the amendment of previous "use" claims into proper method claim form. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 8:00-5:30; every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618